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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,078	07/25/2001	William F. Wade	PM	7302

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,078	WADE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5 and 8-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5, 8-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.
Applicant's submission filed on 2/1/05 has been entered.

Applicant's amendment, filed 2/1/05, has been entered.

Claims 1, 8-10 and 16-17 have been amended.

Claims 6-7 have been canceled.
Claims 3-4 and 18-30 have been canceled previously.

Claims 1, 2, 5 and 8-17 are under consideration in the instant application as they read on the elected invention.

Applicant's election of Group III (claims 1, 2, and 5-17) drawn to a method of enhancing a humoral or CD4 Th1 (DTH, cell-mediated) immune response by administering an antibody-antigen conjugate wherein the antibody binds a dendritic cell antigen and tumor or cancer antigens and an breast cancer antigen with traverse has been acknowledged.

As indicated previously, given applicant's admission that the specific class and type of antigen are obvious variants over one another, the species of classes and types of antigens are held obvious in view of one another in the instant application.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's amendment, filed 2/1/05.
The rejections of record can be found in the previous Office Actions.

3. Upon reconsideration of applicant's amended claims, filed 2/1/05; the priority of the instant claims appears to be the filing date of priority application USSN 60/090,849, filed 6/26/98.

4. Upon reconsideration of applicant's amendment filed 2/1/05, the previous objection to the amendment filed 5/24/04, under 35 U.S.C. 132, new matter with respect to "and gp72", which is disclosed in the replaced paragraph bridging pages 10-11, filed 5/24/04. has been withdrawn.

5. Upon reconsideration of applicant's amended claims to delete the recitation of "synergistically", the previous rejection under 35 U.S.C. 112, first paragraph, enablement, has been withdrawn.

6. Upon reconsideration of applicant's amended claims to delete the recitation of "synergistically", the previous rejection under 35 U.S.C. 112, second paragraph, has been withdrawn.

7. Claims 1, 2, 5 and 8-17 stand rejected under 35 U.S.C.§ 103(a) as being unpatentable over Anand et al. (US 6,291,208 B1) and Heath (US 2002/0135722 A1) and further in view of applicant's admission that species of classes and types of antigens are held obvious in view of one another in the instant application essentially for the reasons of record.

Applicant's arguments, filed 2/1/05, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

Again, applicant asserts that the prior art does not teach nor suggest all three component of the composition used in accordance with the method of the invention, namely (i) an antigen attached to (ii) an antibody that specifically binds to a molecule which is expressed by an antigen-presenting cell and (iii) an anti-CD40 antibody.

These assertions are inconsistent with applicant's acknowledgement that Anand et al. teach the use of antibody conjugates comprising antibodies that bind antigen presenting cells, including dendritic cells to deliver antigens in order to generate immunogenic compositions to a variety of antigens that Heath teaches the co-administration of a CD40 stimulating moiety as an adjuvant in combination with an antigen.

Therefore, the prior art teaching does include all three components of the composition used in the accordance with the method of the invention.

While applicant has asserted that Heath does not teach nor suggest that the co-entrapment on/in a carrier system is an antibody that specifically binds to a molecule which is expressed by an antigen presenting cells and now asserts that Heath does not suggest the use of an antibody to target an antigen to an antigen-presenting cells,
applicant also has acknowledged that combining antigen and/or adjuvant to increase the association between antigen and CD40 binding moiety.

Applicant has argued that Heath does not teach that the antigen is attached to an antibody that targets the antigen to an antigen-presenting cell and that Anand et al. does not teach the use of anti-CD40 antibody.

Again, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Applicant has asserted that one of ordinary skill in the art would not have had a reasonable expectation of producing a synergistic enhancement or suppression of at least the humoral immune response or CD4 Th1 immune response to a target antigen by combining the teaching so the cited references.

A statement or argument by the attorney is not factual evidence.

Again, applicant has not provided objective evidence to support the assertion that the prior art teachings supporting the combination of antibody-antigen conjugates in combination with the adjuvant anti-CD40 would not result in immune responses greater than each element alone.

Adjuvants are substances that enhance or potentiate the immune response to an antigen.

Clearly, the administration of anti-CD40 antibody alone would not enhance or potentiate an immune response to an antigen.

In addition, Heath teach that CD40 stimulators can enhance antibody responses to pneumoccocal polysaccharides in individuals unable to respond to polysaccharide only based vaccines (see Example 5, including paragraph 0126.

Therefore, the prior art does provide an expectation of success in producing an immune response greater than the simple sum of antibody-antigen conjugates and anti-CD40 antibodies acting alone.

Also, as pointed out above; page 36, paragraph 2 of the instant specification further discloses that "if we are to consistently take advantage of the adjuvant or immunosuppressant properties of CD40 ligation, the dynamics of antigen targeting so as to interpose CD40 at the optimal moment or location will need to be determined for the particular antigen system. In this regard, effective manipulation of APC surface molecules in vivo may not be possible".

Therefore, it has not been clear that applicant's reliance on asserted synergistic-type results is consistent with the disclosed Examples and disclosure that "effective manipulation of APC surface molecules in vivo may not be possible" with any antibody-antigen conjugate with anti-CD40 antibodies.

Again, in contrast to applicant's assertions concerning that the prior art does not meet the elements of the claims the following of record is reiterated for applicant's convenience.

Anand et al. teach the use of antibody conjugates comprising antibodies that bind antigen presenting cells, including dendritic cells (e.g. column 2, paragraphs 4 and 6), to deliver antigens in order to generate immunogenic compositions to a variety of antigens (e.g. column 7, paragraph 2) (see entire document, including Summary of the Invention and General Description of the Invention). Anand et al. Teach that these is applicable to any antigen which it is desired to target to antigen presenting cells, including antigens derived from viruses, bacteria and tumors (see column 7, paragraph 1)

Heath teaches the co-administration of a CD40 stimulating moiety (e.g. anti-CD40 antibodies) (e.g., see paragraphs 0055, 0061, 0062) and the appropriate antigen, including the use of covalent linkage or co-entrapment as a vaccine (e.g. see paragraphs 0026-0027 and 0029) to a variety of antigens (see entire document, including Summary of the Invention).

In addition to the variety of antigens as well as the general applicability of antigens as taught by Anand et al. and Heath, applicant's election, filed 11/3/03, notes that the ordinary artisan would reasonably expect that results obtained by the invention with experimental antigens such as hen egg lysozyme and avidin are also predictive of results expected with the invention with regard to antigens associated with any of a large number of pathologies. Given applicant's admission that the specific class and type of antigen are obvious variants over one another, the species of classes and types of antigens are held obvious in view of one another in the instant application.

Also, it is noted that Anand et al. teach that the quantity to be administered depends on the subject to be treated, including the capacity of the individual's immune-system to synthesize antibodies and to produce a cell-mediated immune response (column 9, paragraph 1).

In addition, Heath teaches that providing anti-CD40 with antigen has an advantage for the vaccination of patient with immune deficiencies (paragraph 0126).

Therefore, it would have obvious for the ordinary artisan to enhance immune responses or vaccinate aged or immunocompromised individuals as well as subjects fifty years or older in order to stimulate immune responses or to vaccinate such individuals to a wide variety of antigens based on need. For example, boosting immune responses to a variety of antigens (e.g. pathogens or tumor antigens) in such individuals was known and practiced at the time the invention was made.

Given the teachings of Heath to provide anti-CD40 with antigen in composition form or as a conjugate (see Summary of the Invention) and the teachings of Anand et al. to provide antigen with anti-antigen presenting cell / dendritic cell antibodies; it would have been obvious to one of ordinary skill in the art to administer the antigen in the context of such antigen-antibody conjugate with the immunostimulatory anti-CD40 antibodies to boost the immune response to a wide variety of desired antigens, including providing both components in the same composition, as taught by Heath (see paragraphs 0026-0027 and 0029).

In addition, the motivation to combine the prior art can arise from the expectation that the prior art elements will perform their expected function to achieve their expected results when combined for their common known purpose. Here, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine both antigen-antibody conjugates for dendritic cells and CD40-specific antibodies to target antigens to the antigen presenting cells of interest, including CD40-expressing antigen presenting cells, as well as to enhance the immunogenicity of said antigens.

Given the teachings of Anand et al. and Heath; the ordinary artisan would have been motivated to target professional antigen presenting cells such as dendritic cells with the combination of antigen-antibody targets and the immunostimulatory agonistic CD40 antibodies to enhance the immune response to a wide variety of antigens. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

9. No claim allowed.

10. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
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March 31, 2005